

Remarks

Claims 1-29 and 34-36 and 40-42 have been canceled without prejudice. Claims 30-33, 37-39, and 43-47 are pending. Applicants respectfully acknowledge the allowability of claims 37, 44, 46, and 47 as well as claims 31-33 if written in independent format. Accordingly, applicants have amended claim 31 to be written in independent form. Applicants now believe claims 31-33 to be allowable. Also, applicants have amended claims 30 and 45 as described below. Support for amended claim 45 can be found at least on page 48, lines 10-11. New claim 48 has been added. Support for new claim 48 can be found at least in original claims 1 and 3 and on page 40, lines 26-32; page 48, lines 32-35; and page 49, lines 3-6.

Summary of Interview

Applicant would like to thank the Examiner for his helpful comments during the interview of March 17, 2005. Regarding the written description rejection of claim 45, the Examiner indicated his position focused on the word "about." Applicant acknowledged the Examiner's position, and indicated that they would remove the term from the claim, but would add an additional truncation (150 amino acid truncation) for which applicants have support.

The Examiner also noted that objection to the term "about" was also present in rejected claim 30. Applicant agreed to remove "about" claim 30 as well. Applicants then presented evidence in support of the claimed range that was rejected by the Examiner. The Examiner indicated that if applicants provide the support for the range and arguments indicating why this support is sufficient, the Examiner will review the arguments and also consult with his supervisor regarding the sufficiency of the support.

Lastly, applicants provided evidence to the Examiner in support for the written description rejection of claims 38 and 43. Examiner reviewed applicants' support, and indicated that he would consider the support when presented to him in the present amendment.

35 U.S.C. § 112, first paragraph

Claims 30-33, 38, 39, 43, and 45 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to provide written description to reasonably convey to one of skill in the art to make or use the invention.

In particular, the Examiner has rejected claim 30 for the recitation “about 152-145 carboxy terminal amino acid residues are truncated from the native diphtheria toxin moiety.” The Examiner has rejected claims 38 and 43 for the recitation of “inhibiting rejection of transplanted tissue or organs.” Lastly, the Examiner has rejected claim 45 for the recitation of “about 152 or 145 carboxy terminal amino acid residues.”

1. Regarding the Examiner’s rejection of claim 30, the Examiner states in the November 15, 2004, Office Action that “4 specific truncation mutants provides insufficient support for the range of mutants of the claims.” Applicants respectfully point out that range as currently claimed comprises truncations of 152-145 amino acid residues. DT390, DT383, and MSPΔ5 represent a truncation of 145, 152, and 150 carboxy terminal residues respectively. Thus, applicants have provided description of three working examples within the claimed range. Thus, 3 of the 8 possible mutants (37.5% of the mutants) within the range claimed are exemplified in the specification. Moreover, two of the truncations (145 and 152) represent the ends of the range and a third is a truncation within the claimed range. The Examiner’s stated position in the Office Action of November 15, 2004, is that applicants do not have support for species within the range such as DT151 and DT149. There is no objective basis for this assertion. When the ends of a truncation range are disclosed and shown to have the described function, there is no reason to believe that intermediate truncations will have a different or more/less function. Given the nature of the element at issue, a truncation, the skilled person would recognize from the disclosure of the longest and shortest truncation that all truncations encompassed by the longest and shortest truncation are in applicants’ possession. There is no other way to interpret the teaching of the same function in both the longest and shortest truncation.

Moreover, in the present case, a specific intermediate value is described and exemplified as possessing the same recited function as both the longest and shortest truncations of the recited range. Thus, the objective evidence of the record shows that the longest, shortest, and intermediate values are described. A person of skill in the art would recognize that the disclosure of the longest, the shortest and an intermediate example of a truncation range evidences possession of the other intermediate truncations. Applying the proper objective standard to this issue requires evidence to contradict applicants showing that they are in possession of the full range described. Because such objective evidence is not presented by the

Office, the present rejection is improper. It is not legally necessary to provide description of each and every position within the range to have written support sufficient to convey to one of skill in the art that applicants were in possession of the range at the time the application was filed. In the present situation, requiring additional examples to meet the possession requirement for this type of range amounts to a *de facto* requirement that every value within the range be exemplified. Such a *de facto* requirement is just as improper as a *per se* requirement would be under the proper legal standard.

Furthermore, the Office's own guidelines for written description (*see* MPEP 2163) do not support the position taken in the present case. Applicants remind the Examiner that each value in the claimed "range" is actually a particular species with a very limited genus of truncation mutants. As noted in the MPEP 2163, "the written description requirement for a claimed genus may be satisfied thorough sufficient description of a representative number of species." For example, a truncation of 145 amino acid residues refers to a truncation mutant having the 145 carboxy terminal amino acid residues removed, and a truncation of 152 amino acid residues refers to a truncation mutant having the 152 carboxy terminal amino acid residues removed. Thus, applicants are actually claiming a genus of 8 truncation mutants and provide 3 examples of species that fall within the limited genus of 8 mutants. Clearly 3 species out of 8 possible and immediately envisioned species within a genus is a representative number of species within that genus. Indeed, even a single species can be sufficiently representative to provide descriptive support for the claim of a genus. *In re Herschler*, 591 F.2d 693, 697, 200 USPQ 711, 714 (CCPA 1979) (disclosure of corticosteroid in DMSO sufficient to support claims drawn to a method of using a mixture of a "physiologically active steroid" and DMSO because "use of known chemical compounds in a manner auxiliary to the invention must have a corresponding written description only so specific as to lead one having ordinary skill in the art to that class of compounds. Occasionally, a functional recitation of those known compounds in the specification may be sufficient as that description."). The MPEP further states that the sufficiency of a number of species to represent a claimed genus "depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." The present genus of 8 molecules with disclosed sequences meets this test. The Examiner appears to

be relying on the general misclassification of biological sciences as an “unpredictable art” to push forth the position that only species literally provided for can be claimed. However, as noted above, one of skill in the art would clearly see that if applicants are in possession of the longest and shortest truncations of this genus of 8 truncations as well as an intermediate length species, applicants have envisioned the sequences of the remaining species between the longest and shortest species of the genus. Thus, the remaining species in the range are predictable. It is impossible to envision a scenario where one of skill in the art would not know the sequences of all of the truncation mutants in the range or would not recognize that applicants were in possession of not only the longest and shortest truncations, but all those in between.

Applicants also remind the Examiner that it is not necessary for the applicants to provide literal written description of for the language of the claims. See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1564 (Fed. Cir. 1991), (stating “the description need not be in *ipsis verbis* to be sufficient”). Clearly this range of truncations and these specific truncations are supported by the disclosed mutants. Description for this range can be found at least on page 9, lines 15-19; page 13, lines 13-24, and figures 17 and 18 wherein DT390, DT383, and DT370 are described. Support may also be found on page 39, lines 11-14 and page 48, lines 32-35 which describe the residues to which anti-DT antibodies in human serum are directed. Additionally support may be found on page 48, lines 10-1 which describes MSPΔ5 (a 150 residue truncation mutant) and on page 49, lines 3-6 which describes DT390 being a truncation mutant having only the first 390 of 525 residues (ie., a 145 residue truncation). Applicants believe this rejection to be overcome and respectfully request its withdrawal.

2. In rejecting claims 38 and 43, the Examiner contends that applicants have support for “methods of treating graft versus host disease, leukemias and lymphomas, and AIDS, but not a method of inhibiting a rejection of transplanted tissue or organs.” As presented during the interview of March 17, 2005, applicants respectfully point out that support for a method of inhibiting rejection of transplanted tissue or organs can be found at least on page 31, lines 17-19; page 32, lines 19-26; and page 40, lines 3-5, where the use of immunotoxins to prolong skin graft survival is discussed; page 39, lines 33-35, where the use of the immunotoxins to regress xenografted human T-cell tumors is discussed; page 40, lines 5-7, where the use of immunotoxins induce tolerance to mismatched kidney transplants is discussed (applicants note

that the induction of tolerance would prevent the mounting of an immune response, thus the factors that contribute to rejection of a grafted tissue/organ would be suppressed). Thus, applicants clearly provide description of methods to inhibit graft rejection. Applicants believe this rejection to be overcome and respectfully request its withdrawal.

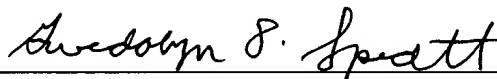
3. Regarding the rejection of claim 45 under 35 U.S.C. 112, first paragraph, applicants have amended claim 45 to remove the term “about” from the claim. Applicants have also added an additional mutant into the claim. Thus, the amended claim now recites “wherein 152, 150, or 145 carboxy terminal amino acid residues.” Support for the 150 amino acid truncation mutant can be found at least on page 48, lines 10-11. In light of the amendment, applicants believe this rejection to be moot and respectfully request its withdrawal.

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application are believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

A Credit Card Payment Form PTO-2038 authorizing payment in the amount of \$450.00 (fee for a two (2) month extension of time), a Request for Extension of Time is enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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Gwendolyn D. Spratt

4-15-05

Date